RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM

16%
OF DIGESTIVE SYSTEM TUMOURS ARE RARE EPITHELIAL TUMOURS

INCIDENCE

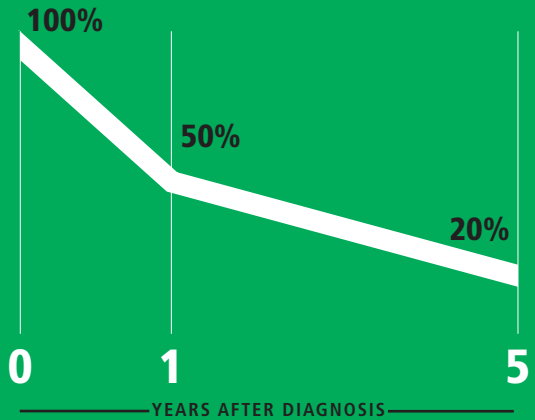
17 532
ESTIMATED NEW CASES
ITALY, 2015

		% OF RARE EPITHELIAL TUMOURS OUT OF ALL TUMOURS IN EACH SITE
2 262	EPITHELIAL TUMOURS OF OESOPHAGUS	81
271	RARE EPITHELIAL TUMOURS OF STOMACH	1
696	EPITHELIAL TUMOURS OF SMALL INTESTINE	56
87	RARE EPITHELIAL TUMOURS OF COLON	<1
97	RARE EPITHELIAL TUMOURS OF RECTUM	1
1 143	EPITHELIAL TUMOURS OF ANAL CANAL	97
71	RARE EPITHELIAL TUMOURS OF PANCREAS	1
7 291	EPITHELIAL TUMOURS OF LIVER AND INTRAHEPATIC BILE TRACT	53
5 483	EPITHELIAL TUMOURS OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT	99
132	MESOTHELIOMA OF PERITONEUM	

PREVALENCE

43 452
ESTIMATED PREVALENT CASES
ITALY, 2010

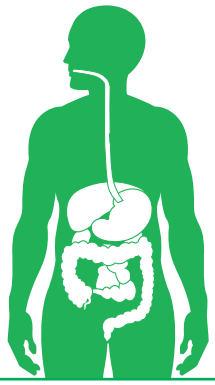
SURVIVAL



SOURCE: AIRTUM. ITALIAN CANCER FIGURES–REPORT 2015

RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM

INCIDENCE



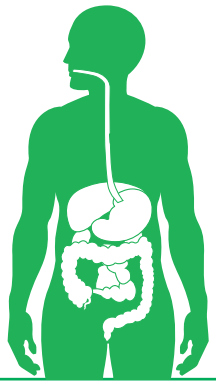
RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM. Crude incidence (rate per 100,000/year) and 95% confidence interval (95% CI), observed cases and proportion of rare cancers on all (common + rare) cancers by site. Rates with 95% CI by sex and age. Estimated new cases at 2015 in Italy.

	AIRTUM POOL (period of diagnosis 2000-2010)														ITALY
					SEX				AGE						
					MALE		FEMALE		0-54 yrs		55-64 yrs		65+ yrs		
	RATE	95% CI	OBSERVED CASES (No.)	RARE EPITHELIAL CANCERS BY SITE (%)	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	RATE	95% CI	ESTIMATED NEW CASES 2015
RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM	**26.11**	**25.89-26.32**	**57 891**	**16%**	**32.11**	**31.78-32.45**	**20.48**	**20.22-20.74**	**3.74**	**3.64-3.83**	**40.15**	**39.40-40.91**	**93.99**	**93.08-94.90**	**17 532**
EPITHELIAL TUMOURS OF OESOPHAGUS	**3.38**	**3.30-3.45**	**7 488**	**81%**	**5.35**	**5.21-5.49**	**1.53**	**1.46-1.60**	**0.63**	**0.59-0.67**	**6.90**	**6.60-7.22**	**10.59**	**10.29-10.90**	**2 262**
Squamous cell carcinoma with variants of oesophagus	2.44	2.37-2.50	5 405		3.74	3.63-3.86	1.21	1.15-1.28	0.47	0.43-0.50	5.43	5.15-5.71	7.33	7.07-7.58	1 619
Adenocarcinoma with variants of oesophagus	0.90	0.86-0.94	1 993		1.54	1.47-1.62	0.30	0.26-0.33	0.15	0.13-0.17	1.41	1.27-1.55	3.14	2.97-3.31	616
Salivary gland type tumours of oesophagus	<0.01	0.00-0.00	4		NE	–	NE	–	NE	–	NE	–	NE	–	2
Undifferentiated carcinoma of oesophagus	0.04	0.03-0.05	86		0.06	0.04-0.07	0.02	0.01-0.03	<0.01	0.00-0.01	0.07	0.04-0.11	0.13	0.10-0.17	27
RARE EPITHELIAL TUMOURS OF STOMACH	**0.40**	**0.37-0.42**	**879**	**1%**	**0.50**	**0.46-0.54**	**0.30**	**0.27-0.33**	**0.06**	**0.05-0.07**	**0.62**	**0.53-0.72**	**1.42**	**1.31-1.53**	**271**
Squamous cell carcinoma with variants of stomach	0.09	0.08-0.11	204		0.14	0.12-0.17	0.04	0.03-0.06	0.01	0.01-0.02	0.18	0.14-0.24	0.31	0.26-0.37	62
Salivary gland type tumours of stomach	<0.01	0.00-0.00	2		NE	–	NE	–	NE	–	NE	–	NE	–	1
Undifferentiated carcinoma of stomach	0.30	0.28-0.33	673		0.35	0.32-0.39	0.26	0.23-0.29	0.05	0.04-0.06	0.43	0.36-0.51	1.11	1.01-1.21	208
EPITHELIAL TUMOURS OF SMALL INTESTINE	**1.02**	**0.98-1.06**	**2 261**	**56%**	**1.15**	**1.09-1.22**	**0.90**	**0.84-0.95**	**0.20**	**0.18-0.22**	**1.40**	**1.26-1.55**	**3.60**	**3.42-3.78**	**696**
Adenocarcinoma with variants of small intestine	0.78	0.74-0.81	1 722		0.91	0.85-0.97	0.65	0.61-0.70	0.16	0.14-0.19	1.19	1.06-1.32	2.62	2.47-2.77	521
Squamous cell carcinoma with variants of small intestine	<0.01	0.01-0.01	21		0.01	0.01-0.02	<0.01	0.00-0.01	<0.01	0.00-0.00	<0.01	0.00-0.03	0.04	0.02-0.06	6
RARE EPITHELIAL TUMOURS OF COLON	**0.13**	**0.12-0.15**	**293**	**0.2%**	**0.11**	**0.09-0.13**	**0.15**	**0.13-0.17**	**0.05**	**0.04-0.06**	**0.18**	**0.14-0.24**	**0.38**	**0.32-0.44**	**87**
Squamous cell carcinoma with variants of colon	0.03	0.03-0.04	74		0.02	0.01-0.03	0.04	0.03-0.06	0.01	0.01-0.02	0.06	0.03-0.09	0.10	0.07-0.13	23
Fibromixoma and low grade mucinous adenocarcinoma of the appendix	0.10	0.09-0.11	219		0.09	0.07-0.11	0.11	0.09-0.13	0.04	0.03-0.05	0.13	0.09-0.18	0.28	0.23-0.33	65
RARE EPITHELIAL TUMOURS OF RECTUM	**0.14**	**0.13-0.16**	**318**	**1%**	**0.08**	**0.06-0.10**	**0.20**	**0.18-0.23**	**0.05**	**0.04-0.06**	**0.20**	**0.15-0.26**	**0.43**	**0.37-0.50**	**97**
Squamous cell carcinoma with variants of rectum	0.14	0.13-0.16	318		0.08	0.06-0.10	0.20	0.18-0.23	0.05	0.04-0.06	0.20	0.15-0.26	0.43	0.37-0.50	97
EPITHELIAL TUMOURS OF ANAL CANAL	**1.69**	**1.64-1.75**	**3 750**	**97%**	**1.40**	**1.33-1.47**	**1.97**	**1.89-2.05**	**0.47**	**0.43-0.50**	**2.53**	**2.35-2.73**	**5.36**	**5.15-5.58**	**1 143**
Squamous cell carcinoma with variants of anal canal	0.92	0.88-0.96	2 042		0.56	0.52-0.61	1.26	1.19-1.32	0.34	0.31-0.37	1.52	1.38-1.68	2.52	2.38-2.68	611
Adenocarcinoma with variants of anal canal	0.60	0.57-0.64	1 338		0.71	0.66-0.77	0.50	0.46-0.54	0.10	0.08-0.12	0.85	0.74-0.96	2.18	2.04-2.32	411
Paget's disease of anal canal	<0.01	0.00-0.01	8		NE	–	NE	–	NE	–	NE	–	NE	–	2
RARE EPITHELIAL TUMOURS OF PANCREAS	**0.11**	**0.10-0.12**	**241**	**1%**	**0.12**	**0.10-0.14**	**0.10**	**0.08-0.12**	**0.04**	**0.03-0.05**	**0.17**	**0.12-0.22**	**0.32**	**0.27-0.38**	**71**
Squamous cell carcinoma with variants of pancreas	0.02	0.01-0.02	39		0.02	0.01-0.03	0.01	0.01-0.02	<0.01	0.00-0.01	0.03	0.01-0.05	0.05	0.03-0.08	12
Acinar cell carcinoma of pancreas	0.04	0.03-0.05	94		0.06	0.05-0.08	0.02	0.02-0.04	0.01	0.01-0.02	0.08	0.05-0.13	0.12	0.09-0.16	28
Mucinous cystadenocarcinoma of pancreas	0.03	0.02-0.03	56		0.02	0.01-0.03	0.03	0.02-0.04	<0.01	0.00-0.01	0.03	0.01-0.06	0.08	0.06-0.11	16
Intraductal papillary mucinous carcinoma invasive of pancreas	0.02	0.01-0.02	34		0.02	0.01-0.03	0.01	0.01-0.02	<0.01	0.00-0.01	0.03	0.01-0.05	0.05	0.03-0.08	10
Solid pseudopapillary carcinoma of pancreas	<0.01	0.00-0.01	13		NE	–	NE	–	NE	–	NE	–	NE	–	4
Serous cystadenocarcinoma of pancreas	<0.01	0.00-0.00	3		NE	–	NE	–	NE	–	NE	–	NE	–	1
Carcinoma with osteoclast-like giant cells of pancreas	<0.01	0.00-0.00	2		NE	–	NE	–	NE	–	NE	–	NE	–	1
EPITHELIAL TUMOURS OF LIVER AND INTRAHEPATIC BILE TRACT	**11.05**	**10.91-11.19**	**24 497**	**53%**	**16.32**	**16.08-16.57**	**6.10**	**5.96-6.25**	**1.53**	**1.47-1.59**	**18.62**	**18.11-19.14**	**38.93**	**38.35-39.52**	**7 291**
Hepatocellular carcinoma of liver and IBT	9.37	9.25-9.50	20 784		14.22	14.00-14.45	4.83	4.70-4.96	1.22	1.17-1.28	15.63	15.17-16.11	33.39	32.85-33.94	6 195
Hepatocellular carcinoma, fibrolamellar of liver and IBT	0.09	0.07-0.10	189		0.13	0.11-0.16	0.04	0.03-0.06	0.01	0.01-0.02	0.13	0.09-0.18	0.30	0.26-0.36	55
Cholangiocarcinoma of IBT	0.90	0.86-0.94	2 003		1.09	1.03-1.16	0.73	0.68-0.78	0.18	0.16-0.20	1.65	1.50-1.81	2.91	2.76-3.08	593
Adenocarcinoma with variants of liver and IBT	0.65	0.61-0.68	1 432		0.83	0.77-0.88	0.48	0.44-0.52	0.11	0.09-0.13	1.14	1.02-1.28	2.17	2.04-2.32	422
Undifferentiated carcinoma of liver and IBT	0.02	0.01-0.02	40		0.02	0.02-0.03	0.01	0.01-0.02	<0.01	0.00-0.01	0.04	0.02-0.07	0.06	0.04-0.09	12
Squamous cell carcinoma with variants of liver and IBT	0.02	0.01-0.02	36		0.02	0.01-0.03	0.01	0.01-0.02	<0.01	0.00-0.00	0.02	0.01-0.04	0.07	0.04-0.09	11
Bile duct cystadenocarcinoma of IBT	<0.01	0.00-0.01	13		NE	–	NE	–	NE	–	NE	–	NE	–	4
EPITHELIAL TUMOURS OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT	**7.99**	**7.87-8.11**	**17 715**	**99%**	**6.84**	**6.68-7.00**	**9.07**	**8.89-9.24**	**0.66**	**0.62-0.70**	**9.15**	**8.79-9.52**	**32.37**	**31.84-32.91**	**5 483**
Adenocarcinoma with variants of gallbladder	2.03	1.97-2.09	4 498		1.31	1.24-1.38	2.71	2.61-2.80	0.20	0.18-0.23	3.14	2.93-3.36	7.59	7.34-7.85	1 328
Adenocarcinoma with variants of EBT	2.24	2.17-2.30	4 960		2.54	2.44-2.64	1.95	1.87-2.04	0.31	0.28-0.34	3.67	3.44-3.90	7.94	7.68-8.21	1 479
Squamous cell carcinoma of gallbladder and EBT	0.04	0.03-0.05	84		0.02	0.02-0.04	0.05	0.04-0.07	<0.01	0.00-0.01	0.06	0.04-0.10	0.14	0.11-0.18	25
MESOTHELIOMA OF PERITONEUM	**0.20**	**0.18-0.22**	**449**	**NA**	**0.25**	**0.22-0.28**	**0.16**	**0.14-0.18**	**0.06**	**0.05-0.07**	**0.38**	**0.31-0.46**	**0.59**	**0.52-0.66**	**132**

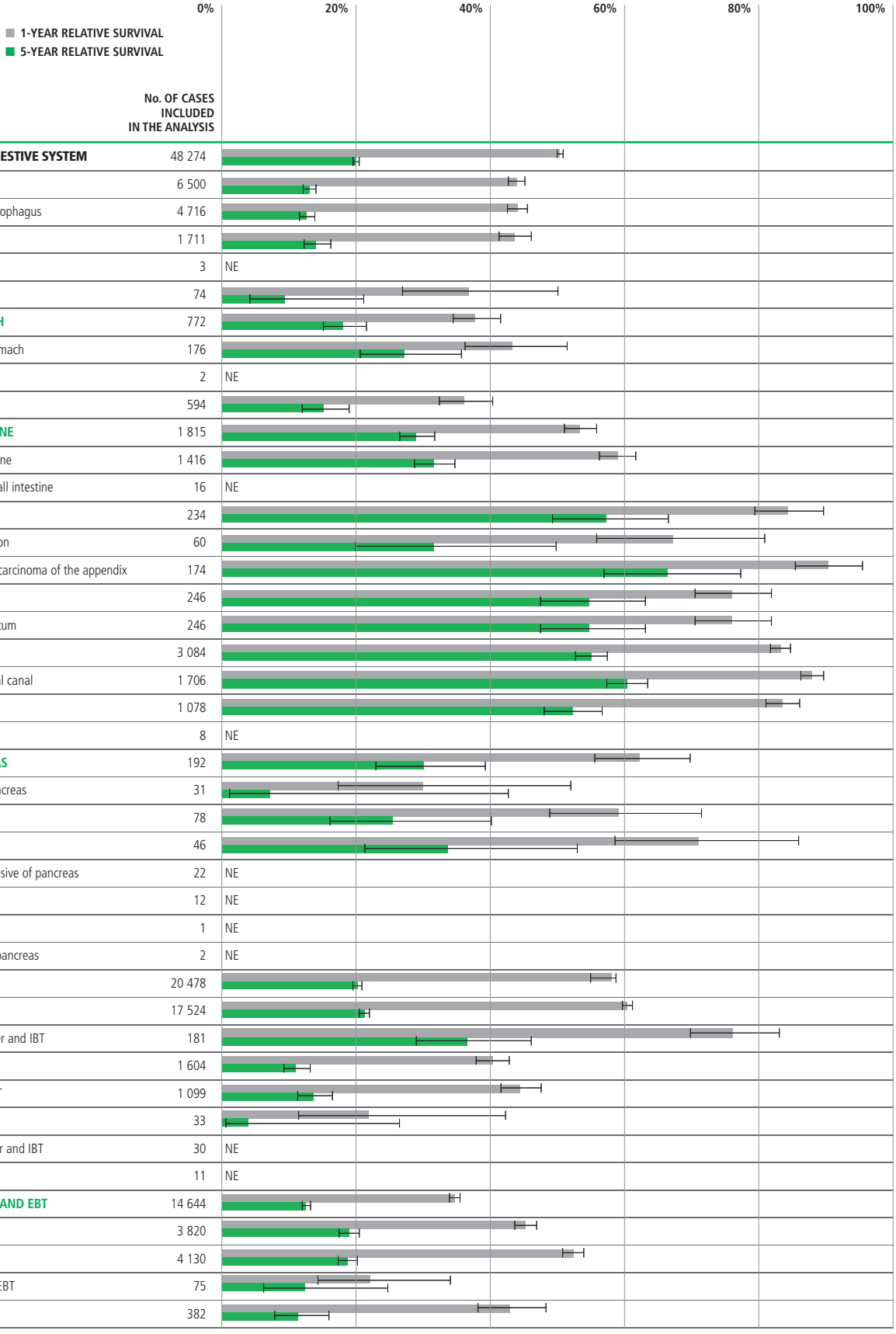
NE: not estimable because 15 or less incident cases were observed **IBT:** intrahepatic bile tract **EBT:** extrahepatic bile tract **NA:** not applicable

RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM

SURVIVAL



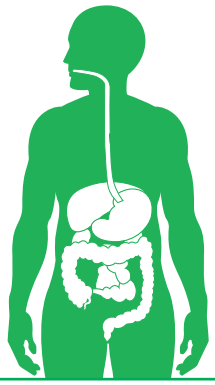
RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM. One and 5-year relative survival. Error bars are 95% confidence interval. Cohort approach (complete analysis), period of diagnosis 2000-2008.



	No. OF CASES INCLUDED IN THE ANALYSIS
RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM	48 274
EPITHELIAL TUMOURS OF OESOPHAGUS	6 500
Squamous cell carcinoma with variants of oesophagus	4 716
Adenocarcinoma with variants of oesophagus	1 711
Salivary gland type tumours of oesophagus	3
Undifferentiated carcinoma of oesophagus	74
RARE EPITHELIAL TUMOURS OF STOMACH	772
Squamous cell carcinoma with variants of stomach	176
Salivary gland type tumours of stomach	2
Undifferentiated carcinoma of stomach	594
EPITHELIAL TUMOURS OF SMALL INTESTINE	1 815
Adenocarcinoma with variants of small intestine	1 416
Squamous cell carcinoma with variants of small intestine	16
RARE EPITHELIAL TUMOURS OF COLON	234
Squamous cell carcinoma with variants of colon	60
Fibromixoma and low grade mucinous adenocarcinoma of the appendix	174
RARE EPITHELIAL TUMOURS OF RECTUM	246
Squamous cell carcinoma with variants of rectum	246
EPITHELIAL TUMOURS OF ANAL CANAL	3 084
Squamous cell carcinoma with variants of anal canal	1 706
Adenocarcinoma with variants of anal canal	1 078
Paget's disease of anal canal	8
RARE EPITHELIAL TUMOURS OF PANCREAS	192
Squamous cell carcinoma with variants of pancreas	31
Acinar cell carcinoma of pancreas	78
Mucinous cystadenocarcinoma of pancreas	46
Intraductal papillary mucinous carcinoma invasive of pancreas	22
Solid pseudopapillary carcinoma of pancreas	12
Serous cystadenocarcinoma of pancreas	1
Carcinoma with osteoclast-like giant cells of pancreas	2
EPITHELIAL TUMOURS OF LIVER AND IBT	20 478
Hepatocellular carcinoma of liver and IBT	17 524
Hepatocellular carcinoma, fibrolamellar of liver and IBT	181
Cholangiocarcinoma of IBT	1 604
Adenocarcinoma with variants of liver and IBT	1 099
Undifferentiated carcinoma of liver and IBT	33
Squamous cell carcinoma with variants of liver and IBT	30
Bile duct cystadenocarcinoma of IBT	11
EPITHELIAL TUMOURS OF GALLBLADDER AND EBT	14 644
Adenocarcinoma with variants of gallbladder	3 820
Adenocarcinoma with variants of EBT	4 130
Squamous cell carcinoma of gallbladder and EBT	75
MESOTHELIOMA OF PERITONEUM	382

NE: not estimable because 30 or less incident cases were observed **IBT:** intrahepatic bile tract **EBT:** extrahepatic bile tract

PREVALENCE



RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM. Observed prevalence (proportion per 100,00 and 95% confidence interval - 95% CI) by duration (≤2, 2-5, ≤15 years) prior to prevalence date (1st January 2007), and complete prevalence. Estimated prevalent cases in 2010 in Italy.

	AIRTUM POOL								ITALY
	OBSERVED PREVALENCE BY DURATION						COMPLETE PREVALENCE		
	≤2 YEARS		2-5 YEARS		≤15 YEARS				ESTIMATED PREVALENT CASES 2010
	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI	PROPORTION	95% CI	
RARE EPITHELIAL TUMOURS OF THE DIGESTIVE SYSTEM	**28.41**	**27.3-29.55**	**17.74**	**16.87-18.65**	**65.73**	**64.04-67.46**	**74.38**	**71.54-75.42**	**43 452**
EPITHELIAL TUMOURS OF OESOPHAGUS	**3.69**	**3.30-4.12**	**1.69**	**1.43-1.98**	**7.72**	**7.15-8.33**	**8.70**	**8.04-9.36**	**5 013**
Squamous cell carcinoma with variants of oesophagus	2.63	2.30-3.00	1.16	0.94-1.41	5.54	5.05-6.06	6.31	5.74-6.87	3 629
Adenocarcinoma with variants of oesophagus	1.03	0.83-1.26	0.48	0.35-0.65	2.09	1.80-2.42	2.28	1.95-2.61	1 319
Salivary gland type tumours of oesophagus	NE	–	NE	–	NE	–	NE	–	NE
Undifferentiated carcinoma of oesophagus	0.03	0.01-0.10	0.05	0.01-0.12	0.09	0.04-0.18	0.11	0.03-0.19	65
RARE EPITHELIAL TUMOURS OF STOMACH	**0.21**	**0.13-0.33**	**0.17**	**0.09-0.28**	**0.82**	**0.64-1.03**	**0.96**	**0.73-1.18**	**556**
Squamous cell carcinoma with variants of stomach	0.05	0.01-0.12	0.09	0.04-0.18	0.34	0.23-0.48	0.36	0.23-0.49	207
Salivary gland type tumours of stomach	NE	–	NE	–	NE	–	NE	–	NE
Undifferentiated carcinoma of stomach	0.17	0.09-0.28	0.07	0.03-0.16	0.48	0.35-0.65	0.59	0.41-0.78	349
EPITHELIAL TUMOURS OF SMALL INTESTINE	**1.02**	**0.82-1.26**	**0.87**	**0.69-1.09**	**3.16**	**2.80-3.56**	**4.35**	**3.83-4.88**	**2 517**
Adenocarcinoma with variants of small intestine	0.86	0.68-1.08	0.79	0.61-1.00	2.79	2.45-3.16	3.77	3.29-4.26	2 187
Squamous cell carcinoma with variants of small intestine	0.01	0.00-0.06	NE	–	0.02	0.00-0.08	0.04	0.00-0.10	23
RARE EPITHELIAL TUMOURS OF COLON	**0.24**	**0.15-0.37**	**0.25**	**0.16-0.38**	**0.83**	**0.65-1.04**	**0.92**	**0.71-1.14**	**589**
Squamous cell carcinoma with variants of colon	0.02	0.00-0.08	0.02	0.00-0.08	0.08	0.03-0.17	0.10	0.03-0.17	58
Fibromixoma and low grade mucinous adenocarcinoma of the appendix	0.22	0.13-0.34	0.23	0.14-0.35	0.75	0.58-0.95	0.83	0.62-1.03	531
RARE EPITHELIAL TUMOURS OF RECTUM	**0.23**	**0.14-0.36**	**0.18**	**0.11-0.30**	**0.80**	**0.62-1.01**	**1.10**	**0.83-1.37**	**651**
Squamous cell carcinoma with variants of rectum	0.23	0.14-0.36	0.18	0.11-0.30	0.80	0.62-1.01	1.10	0.83-1.37	651
EPITHELIAL TUMOURS OF ANAL CANAL	**3.01**	**2.66-3.40**	**2.79**	**2.45-3.16**	**10.11**	**9.45-10.80**	**13.24**	**12.36-14.13**	**7 735**
Squamous cell carcinoma with variants of anal canal	1.85	1.58-2.16	1.92	1.64-2.23	6.57	6.04-7.13	9.18	8.41-9.94	5 397
Adenocarcinoma with variants of anal canal	1.05	0.84-1.28	0.76	0.58-0.96	3.05	2.69-3.44	3.81	3.35-4.28	2 196
Paget's disease of anal canal	NE	–	0.01	0.00-0.06	0.05	0.01-0.12	0.06	0.00-0.11	34
RARE EPITHELIAL TUMOURS OF PANCREAS	**0.14**	**0.07-0.24**	**0.15**	**0.08-0.26**	**0.40**	**0.28-0.56**	**0.57**	**0.37-0.76**	**329**
Squamous cell carcinoma with variants of pancreas	NE	–	0.01	0.00-0.06	0.05	0.01-0.12	0.08	0.00-0.16	45
Acinar cell carcinoma of pancreas	0.06	0.02-0.13	0.09	0.04-0.18	0.17	0.10-0.28	0.24	0.11-0.36	138
Mucinous cystadenocarcinoma of pancreas	0.02	0.00-0.08	0.04	0.01-0.10	0.11	0.06-0.21	0.17	0.06-0.27	97
Intraductal papillary mucinous carcinoma invasive of pancreas	0.05	0.01-0.12	0.01	0.00-0.06	0.06	0.02-0.13	0.07	0.01-0.14	42
Solid pseudopapillary carcinoma of pancreas	0.01	0.00-0.06	NE	–	0.01	0.00-0.06	0.01	0.00-0.03	7
Serous cystadenocarcinoma of pancreas	NE	–	NE	–	NE	–	NE	–	NE
Carcinoma with osteoclast-like giant cells of pancreas	NE	–	NE	–	NE	–	NE	–	NE
EPITHELIAL TUMOURS OF LIVER AND INTRAHEPATIC BILE TRACT	**13.32**	**12.56-14.10**	**8.09**	**7.57-8.78**	**27.12**	**26.04-28.24**	**27.97**	**26.68-28.94**	**16 092**
Hepatocellular carcinoma of liver and IBT	11.86	11.15-12.61	7.46	7.08-8.25	24.82	23.78-25.89	25.55	24.47-26.63	14 690
Hepatocellular carcinoma, fibrolamellar of liver and IBT	0.03	0.01-0.10	0.08	0.05-0.20	0.14	0.07-0.24	0.18	0.07-0.28	103
Cholangiocarcinoma of IBT	0.98	0.79-1.22	0.33	0.20-0.45	1.55	1.30-1.83	1.60	1.33-1.87	922
Adenocarcinoma with variants of liver and IBT	0.43	0.31-0.60	0.21	0.03-0.16	0.59	0.44-0.77	0.61	0.44-0.77	347
Undifferentiated carcinoma of liver and IBT	NE	–	NE	–	NE	–	NE	–	NE
Squamous cell carcinoma with variants of liver and IBT	NE	–	0.02	0.00-0.08	0.02	0.00-0.08	0.03	0.00-0.08	19
Bile duct cystadenocarcinoma of IBT	NE	–	NE	–	0.01	0.00-0.06	0.02	0.00-0.05	11
EPITHELIAL TUMOURS OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT	**6.40**	**5.88-6.95**	**3.48**	**3.00-3.79**	**14.46**	**13.68-15.29**	**16.65**	**15.73-17.57**	**9 669**
Adenocarcinoma with variants of gallbladder	1.98	1.69-2.30	1.43	1.14-1.64	5.64	5.15-6.16	6.52	5.94-7.10	3 792
Adenocarcinoma with variants of EBT	2.55	2.23-2.91	1.60	1.37-1.92	5.98	5.47-6.51	6.76	6.18-7.34	3 887
Squamous cell carcinoma of gallbladder and EBT	0.03	0.01-0.10	NE	–	0.05	0.01-0.12	0.05	0.00-0.10	29
MESOTHELIOMA OF PERITONEUM	**0.16**	**0.09-0.27**	**0.11**	**0.07-0.23**	**0.38**	**0.26-0.54**	**0.52**	**0.34-0.70**	**300**

NE: not estimable in observed prevalence if no cases were observed within ≤2, 2-5, ≤15 years prior to prevalence date, in complete prevalence if the 15-year prevalence is NE

IBT: intrahepatic bile tract **EBT:** extrahepatic bile tract

This group includes epithelial tumours of:
- **oesophagus** (squamous cell carcinoma, adenocarcinoma, salivary gland type, undifferentiated carcinoma);
- **stomach** (squamous cell carcinoma, salivary gland type, undifferentiated carcinoma);
- **small intestine** (adenocarcinoma and squamous cell carcinoma);
- **colon** (squamous cell carcinoma, fibromyxoma and low grade mucinous adenocarcinoma of appendix);
- **rectum** (squamous cell carcinoma);
- **anal canal** (squamous cell carcinoma, adenocarcinoma, Paget's disease);
- **liver and intrahepatic bile duct** (hepatocellular carcinoma, fibrolamellar hepatocellular carcinoma, cholangiocarcinoma, adenocarcinoma, undifferentiated carcinoma, squamous cell carcinoma, bile duct cystoadenocarcinoma);
- **gallbladder and extrahepatic biliary tract** (adenocarcinoma, squamous cell carcinoma);
- **pancreas** (squamous cell carcinoma, acinar cell carcinoma, mucinous cystoadenocarcinoma, intraductal papillary mucinous carcinoma, serous cystoadenocarcinoma, carcinoma with osteoclastic-like giant cells, solid pseudopapillary carcinoma).

Among the rare cancers of the digestive tract we also describe
- **peritoneal mesothelioma**.

All together, rare epithelial cancers account for 16% of all cancers of the digestive system. Non epithelial tumours such as neuroendocrine tumours or sarcomas of the digestive system are not included here but in the sarcoma (p. 84) and neuroendocrine tumour (p. 90) groupings described in this monograph.

RARE EPITHELIAL TUMOURS OF STOMACH, COLON AND RECTUM AND EPITHELIAL TUMOURS OF OESOPHAGUS, SMALL INTESTINE AND ANAL CANAL

WHAT DO WE KNOW ABOUT THESE CANCERS?

All these cancers share similar risk factors: smoking, alcohol, and lifestyle habits, such as consumption of red meat, flour, and refined sugars, overweight, and limited physical activity.[1] Additional site-specific risk factors are: exposure to mycotoxins, human papillomavirus (HPV)[2] infection, and familial predisposition for squamous cell carcinoma of oesophagus; Barrett's oesophagus, gastroesophageal reflux, and bile reflux for adenocarcinoma of oesophagus;[3] Helicobacter pylori (HP) for epithelial tumours of stomach;[4] Crohn's disease, familial adenomatous polyposis for small intestine;[5] family history and hereditary syndromes for colon;[6] HPV infection (strains 16 and 18) for anal canal.

In the oesophagus squamous cell carcinoma is more frequent in the upper middle third part while adenocarcinoma occurs mainly in the lower third because of the different risk factors.

In the stomach squamous cell carcinoma and salivary gland type tumours are very rare. Undifferentiated carcinoma of the stomach is characterised by lesions that lack any differentiated features beyond an epithelial phenotype.

In the small intestine adenocarcinoma is the most common histotype and is located mainly in the second part of the duodenum. Diagnosis is often difficult, but recently videocapsule endoscopy has shown promising results in the diagnosis of disorders and tumours of the small intestine.

Rectal squamous cell carcinoma is more aggressive than adenocarcinoma and has a worse prognosis.

Anal canal cancers, because of their localisation, are often diagnosed when the disease is localised to the locoregional area. It has been shown that chemoradiation in squamous cell carcinoma of the anal canal may offer a good chance of cure without surgery. On the contrary, all other sites are rarely diagnosed as a localised disease. The number of randomised trials is scarce and the data to support evidence-based decisions are very limited. No effective and satisfactory treatment for this disease really exists, thus it is recommended to refer patients with these rare cancers to specialised centres.

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

All epithelial tumours of the **oesophagus** are rare even if all together the epithelial tumours represent the 81% of all the tumours of the oesophagus. All epithelial tumours of the **small intestine** and of the **anal canal** are rare and represent the 56% and 97% of all tumours of small intestine and anal canal, respectively (incidence table, p. 44). In the stomach, colon, and rectum, rare epithelial cancers are 1.5%, 0.2%, and 1%, respectively, based on AIRTUM data.

The most frequent rare epithelial histotype is squamous cell carcinoma, but even common adenocarcinomas in some sites (oesophagus, small intestine, and anal canal) are rare. Most **rare epithelial cancers of the colon** are low grade mucinous adenocarcinoma of the appendix. The other histotypes (salivary gland type tumours, Paget's disease) are extremely rare. Squamous cell carcinoma is more frequent than adenocarcinoma in the oesophagus and anal canal; in the small intestine it is the opposite. We found an unexpectedly high frequency of adenocarcinomas among anal canal cancers. In hospital series they are exceptional, suggesting that some low rectal cancers were classified generically as anal canal cancers.

Rare epithelial tumours of the oesophagus, stomach, and small intestine are more common in males than females. The opposite is true for rare epithelial tumours of the colon, rectum, and anal canal. All these tumours are typical of old ages (>65 years old). Italian and European data of the RARECAREnet database (www.rarecarenet.eu) are similar, but in Italy the incidence of adenocarcinoma of the oesophagus is lower than in Europe and the incidence of adenocarcinoma of the anus is higher.

Survival

Survival of epithelial tumours of the oesophagus, stomach, and small intestine is poor. Five-year relative survival (RS) for these sites, regardless of the histotype, is 13% for the oesophagus, 18% for the stomach, and 29% for the small intestine. RS of rare epithelial tumours of the colon, rectum, and anal canal is slightly better, with almost half of patients alive after 5 years from diagnosis. However, squamous cell carcinoma of the colon has a 5-year RS of 31%, while that of low grade mucinous adenocarcinoma of the appendix is 66% (survival figure, p. 45). Thus, the latter mainly influence the survival of rare epithelial tumours of the colon. Italian and European data of the RARECAREnet database are similar.

Prevalence

About 7,700 persons were estimated to be living with a diagnosis of anal canal tumour (about two thirds with squamous cell carcinomas) at the beginning of 2010. Persons living with a diagnosis of **rare epithelial tumours of the oesophagus** were about 5,000; among these, squamous cell carcinomas are the most frequent (mainly for their relatively high incidence).

Persons with a diagnosis of **small intestine tumours** were about 2,500 (87% with adenocarcinoma). Estimated numbers of prevalent cases of **rare tumours of the stomach, colon, and rectum** were 550, 600, and 650, respectively. Among prevalent cases, the proportion of patients that survived more than 15 years from diagnosis is similar among sites, lower than 30%. Prevalence estimates are coherent with the relatively low incidence and poor prognosis of the majority of these tumours. Prevalence estimates for the oesophagus are a bit higher than those published in the AIRTUM monograph on prevalence[7] because of the different methodology used (see «Materials and methods», pp. 14-21). The other sites are difficult to compare with published data because rare epithelial tumours represent only a small fraction of all the tumours of the site.

RARE EPITHELIAL TUMOURS OF PANCRES

WHAT DO WE KNOW ABOUT THESE CANCERS?

Pancreatic cancer is an aggressive disease with an extremely poor prognosis. It is mainly diagnosed in advanced stage; however, increased use of radiological modalities has led to incidental findings of pancreatic cancer, as well as the detection of precursor lesions which can be monitored and/or resected as necessary. A combination of biochemical tests, radiological imaging, endoscopic ultrasound fine needle aspiration and multidisciplinary discussion in specialised centres is necessary for accurate diagnosis, staging, and for the definition of the appropriate management plan. An example of this approach is the experience of the Province of Reggio Emilia (Emilia-Romagna Region, Central Italy), where since 2012 it has been possible to submit all cases of pancreatic tumours that access the various hospitals in the province to multidisciplinary discussion, both through regular meetings and using a specially created discussion blog.

Risk factors include:[8] excess body weight, chronic inflammation of the pancreas, diabetes, family history of genetic syndromes, personal or family history of pancreatic cancer, smoking.

Squamous cell carcinoma clinical presentation is similar to that of adenocarcinoma.

Acinar cell carcinoma shows different clinical symptoms at presentation, different morphological features, different outcomes, and different molecular alterations, creating difficulties in the clinical and pathological diagnosis and in the therapeutic choice.[9] **Mucinous cystadenocarcinoma** is the malignant form of a mucinous cystic neoplasm. Correct and early characterisation of a premalignant or malignant mucinous cystic neoplasm with surgical resection offers a favourable prognosis. However, once it has become invasive or metastasised, the outcome of a cystic pancreatic carcinoma is poor.

Intraductal papillary mucinous carcinomas comprise a histologic spectrum ranging from adenoma with mild dysplasia to invasive carcinoma. Although the overall outcome is good, a significant proportion of resected patients develop pancreatic adenocarcinoma in the pancreatic remnant.

Solid pseudopapillary carcinoma derives from a solid-pseudopapillary neoplasm; it has been recognised with increasing frequency in recent years. It is characterised by tumour recurrence and/or metastasis.

Serous cystadenocarcinoma of the pancreas is a malignant cystic tumour which, in most cases, shows synchronous or metachronous liver metastases.

Carcinoma with osteoclast-like giant cells is an extraskeletal tumour containing multinucleated osteoclast-like giant cells, which morphologically resemble those found in giant cell tumours of the bone. The clinical features of these tumours remain obscure, as many cases are already advanced when detected. Long-term follow-up of patients with these rare tumours is essential in order to compile a body of literature to help guide treatment, since the rarity of this tumour renders prospective studies unlikely. The development of specialist registries can strongly contribute to the study of pancreatic diseases and the identification of an appropriate approach for diagnosis and treatment.

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

Rare epithelial cancers include several histotypes, which all together represent only 1% of pancreatic tumours. The proportion of rare cancers is so low partly because histological proof is not always obtained. In the AIRTUM database less than 50% of cases have histological verification. This is a problem which leads to an underestimation of the rare histotypes of the pancreas. In addition, 57% of pancreatic cancers have a non-specified morphology, which means that often pathologists do not report/identify the specific histotype, contributing to underestimate the real incidence of rare tumours.

In Italy in the AIRTUM database, in 11 years, 241 cases of rare epithelial tumours of pancreas were observed. The most common histotype is acinar cell carcinoma (39% of cases), followed by mucinous cystadenocarcinoma (23%), squamous cell carcinoma (16%), and invasive intraductal papillary mucinous carcinoma (14%). The other histotypes are extremely rare, with 13 or fewer cases observed in 11 years. Rare epithelial pancreatic cancers are more frequent in males than females and are typical of old age (65-75 years old). Italian and European (RARECAREnet database) are similar.

Survival

Survival of rare epithelial pancreatic cancers is low for all histotypes. Mucinous cystoadenocarcinoma and acinar cell carcinoma have the best 5-year relative survival (RS), which, in any case, is 33% and 25%, respectively. The number of cases of the other histotypes is not enough to provide reliable estimates (see figure p. 45). However, the estimates of the wider RARECAREnet database confirm the poor prognosis expected for solid pseudopapillary carcinoma, which has a 5-year RS of 65% (based on 42 cases only). Again, in the RARECAREnet database the number of cases was not enough to estimate the RS of serous cystadenocarcinoma and carcinoma with osteoclast-like giant cells.

Prevalence

Slightly more than 300 people were estimated to be alive in 2010 with a diagnosis of rare epithelial tumours of the pancreas, with acinar cell

carcinomas being the most prevalent cases (42%). The prevalence estimates are low because of the rarity and poor prognosis of these tumours.

EPITHELIAL TUMOURS OF LIVER AND INTRAHEPATIC BILE DUCT AND OF GALLBLADDER AND EXTRAHEPATIC BILIARY TRACT

WHAT DO WE KNOW ABOUT THESE CANCERS?

Over 70% of primary liver cancers are attributable to Hepatitis C virus (HCV), Hepatitis B virus (HBV), alcohol, smoking, and, for cholangiocarcinoma, primary sclerosing cholangitis (PSC), cirrhosis, diabetes, obesity, and Caroli's disease.[10,11]

For gallbladder cancer the most common risk factors are gallstones, porcelain gallbladder, gallbladder adenoma, bile duct cysts, and abnormalities of the biliopancreatic junction. The risk increases in the case of obesity and a diet high in carbohydrates and low in fibres.

For cancer of the bile ducts the risk factors are chronic inflammation of the bile duct, bile duct cysts, congenital dilatation of intrahepatic bile ducts and cirrhosis.[12]

Histological proof is not always easy to obtain for these sites. Liver, extrahepatic bile duct, and gallbladder are not easily accessible, therefore biopsy and surgery are infrequently performed. In the absence of histological verification, diagnosis is based on operative findings or medical imaging. In the AIRTUM database, 60% of patients have a liver cancer and 40% have a gallbladder cancer diagnosed without histological verification. The proportion of unspecified morphology is high (>40%) and increases in older people (>65 years). Thus, some concerns regarding our analysis should be noted, as the high proportion of unspecified morphology may lead to underestimation of rare liver and gallbladder cancers (which are defined by the combination of topography and morphology). The accuracy of diagnosis of these tumours should increase regardless of the poor prognosis of liver cancers.

THE EPIDEMIOLOGICAL DATA IN ITALY

Incidence

All epithelial tumours of liver and gallbladder are rare because rare cancers are defined on the basis of the European population and not of the country-specific incidence rate. Thus, even hepatocellular carcinoma of the liver and all tumours of the gallbladder, which in Italy are not perceived as rare, fall into the rare category, since in Europe their incidence is 3 and 4 per 100,000, respectively.

Among the **epithelial tumours of liver and intrahepatic bile duct** (IBTs), the hepatocellular is the most frequent (85%) followed by cholangiocarcinoma (8%), and adenocarcinoma (6%) (see table p. 44). Around 200 cases of fibrolamellar hepatocellular carcinoma were observed in 11 years in the AIRTUM database. The other entities are extremely rare. All histotypes are more common in males than females and are typical of the older age group (>65 years). The incidence of all epithelial tumours of the liver does not include the unspecified morphology, which for this site is high. All liver histotypes show higher rates in Italy than in Europe (RARECAREnet database).

Epithelial tumours of gallbladder and extrahepatic bile duct (EBTs) are mainly adenocarcinomas; only 84 cases of squamous cell carcinoma were observed in 11 years in the AIRTUM database. Even in these sites there is a high proportion of unspecified morphologies, however, contrary to liver cancers, the incidence of epithelial tumours of the gallbladder includes the unspecified types (this is the reason why the sum of the proportion of adenocarcinomas of the gallbladder and EBTs do not add up to 100%). The incidence is slightly higher in females, especially for gallbladder tumours and increases with age. The incidence in Italy is slightly higher than in Europe (RARECAREnet database).

Survival

Prognosis of epithelial tumours of the liver, IBTs, epithelial tumours of the gallbladder, and EBTs is poor. One-year RS is 76% and 58% for fibrolamellar hepatocellular carcinoma and hepatocellular carcinoma, respectively. However for all other epithelial tumours of the liver and gallbladder, IBTs, and EBTs, 1-year RS is ≤44%. Survival drops to ≤20% 5 years after diagnosis (except for fibrolamellar hepatocellular carcinoma, for which it is 36%) (see figure p. 45). Survival estimates of undifferentiated carcinoma, squamous cell carcinoma, and bile duct cystadenocarcinoma of liver and IBTs are based on a limited number of cases. In Italy, survival for all these tumours is slightly higher than in Europe, probably because of the screening of high-risk patients (chronic HCV or HBC infection). Moreover, great attention is paid in Italy to the prevention of viral infections through blood work and blood products, donated organs and tissues, and all medical and surgical procedures.

Prevalence

Around 16,000 people were estimated to be alive in Italy in 2010 with a diagnosis of epithelial tumours of the liver. The prevalent cases are mainly due to the relatively high incidence of hepatocellular carcinomas. These data are slightly lower than those presented in the AIRTUM monograph on prevalence,[7] because we do not include cases with unspecified morphology of the liver, which are a high number. Around 9,700 people were estimated to be alive with a diagnosis of epithelial tumours of the gallbladder and were mainly people with adenocarcinomas of gallbladder and EBTs.

MESOTHELIOMA OF PERITONEUM

WHAT DO WE KNOW ABOUT THESE CANCERS?

Peritoneal mesothelioma can have the same morphology as pleural forms (epithelioid, sarcomatoid, and mixed). The tumour may grow, giving only nonspecific signs and symptoms. Patients with peritoneal mesothelioma access different hospital departments from those used by patients with lung mesothelioma. Thus, many different structures must be investigated in epidemiological survey of these tumours (internal medicine and general surgery, as well as thoracic surgery).

Asbestos is the main risk factor for peritoneal mesothelioma. An additional risk factor is radiation used for diagnosis and treatment (Thorotrast) and irradiation of abdominal lymph nodes in prostate cancer.[13] People exposed to asbestos have a risk of mesothelioma of the peritoneum that appears to constantly grow over time, even after cessation of exposure.

THE EPIDEMIOLOGICAL DATA IN ITALY

Only 449 cases of mesothelioma of the peritoneum were observed in the AIRTUM database in 11 years. One-year RS is 43% and drops to 11% at five years. In some population-based studies, a shorter median survival was observed in peritoneal as compared with pleural mesothelioma, but in others there were contrasting results. A possible explanation is that peritoneal mesothelioma has both a shorter survival in most cases and a larger proportion of long-term survivors.[14]

GENERAL REMARKS

In general, if you consider the number of observed cases in the AIRTUM database during the period 2000-2010 and expected cases in 2015 (see table p. 44), you may notice that there are entities with less than 100 yearly diagnosed patients in Italy. The treatment of rare neoplastic conditions is challenging, especially because studies providing high levels of evidence are often lacking especially for the small number of incident cases.[15]

The current reality, for better or for worse, is that patients with a rare tumour consult different hospital centres, and thus the already few incident cases disperse more; also, each hospital centre may lead to use different existing therapies off-label, and although the response to such treatments may be either overwhelmingly positive or negative, there is currently no systematic way to collect this clinical information and learn from it. The creation of a network of centres that deal with special rare cancers, capitalizing on the access of patients in all centres, could serve as a basis to accumulate and consolidate knowledge of the natural history, molecular biology, and treatment of rare cancers: as more drugs and treatments for rare cancers emerge, there will still remain a need for randomised trials or observational studies to compare strategies.[16]

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